UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/535,364 | 03/24/2000 | Michael J. Comb | NEB-138-CIP | 2664 |

31012 7590 11/12/2003

JAMES GREGORY CULLEM, ESQ.
INTELLECTUAL PROPERTY COUNSEL
CELL SIGNALING TECHNOLOGY, INC.
166B CUMMINGS CENTER
BEVERLY, MA 01915

| EXAMINER | |
|---|---|
| PONNALURI, PADMASHRI | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1639 | 22 |

DATE MAILED: 11/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/535,364 | Applicant(s) COMB ET AL. | |
|---|---|---|---|
| | Examiner Padmashri Ponnaluri | Art Unit 1639 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *08 August 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *19,21,22 and 28-39* is/are pending in the application.

4a) Of the above claim(s) *19,21,22 and 34-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-33, 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

NOTE the change of examiner in this application.

### *Status of Application*

The response filed on 8/8/03 has been fully considered and entered into the application.

### *Election/Restrictions*

Applicants in the response filed on 8/8/03 and during the telephonic Interview conducted on 6/9/03, have addressed the restriction between the phosphorylated kinase consensus motif binding antibody and the phosphorylated protein-protein motif binding antibody is not proper. And further stated that the antibody binding to the phosphorylated kinase consensus motif are not distinct, but are structurally similar and share common characteristics (see the response filed on 8/8/03, page 8). And especially in the last paragraph (response filed on 8/8/03, page 8) applicants state that both the antibodies (phosphorylated kinase consensus motif binding antibody and the phosphorylated protein-protein motif binding antibody ) contain one or more fixed residues, including one or more phosphorylated residues; both occur in multiple proteins within a genome. Applicants argue that the subject matter of claim 28 is a genus not requiring further restriction. Applicants in the interview conducted on 6/9/03 have informed that 'the art which reads on the antibody that binds to phosphorylated kinase consensus motif would read on the antibody which binds to the phosphorylated protein-protein binding motif.' In response to applicants arguments that the antibody binding to the phosphorylated kinase consensus motif and antibody binding to the phosphorylated protein-protein binding motif are considered as obvious species and the restriction has been withdrawn.

This application contains claims 19, 21-22 and 34-38 are drawn to an invention nonelected with traverse in Paper No. 13. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

***Status of the claims***

Claim 27 has been deleted and new claim 39 has been added by the amendment filed on 8/8/03. Claims 19, 21-22, 28-39 are currently pending in this application. Claims 19, 21-22 and 34-38 have been withdrawn from further consideration. Claims 28-33 and 39 are currently being examined in this application.

***Objections to the specification and the Claims***

The objection to the abstract and the specification and claim 32 have been withdrawn in view of the amendments filed on 8/8/03.

***Maintained Claim Rejections***

Claims 27-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement as set forth in the previous office action mailed on 2/25/03.

The rejection of claims 28 and 32 (B) as being indefinite under 35 U S C 112, second paragraph are maintained for the reasons of record set forth in the previous office action mailed on 2/25/03.

Claims 27-33 are rejected under 35 U.S.C. 102(e) as being anticipated by Tani et al (US Patent 6,001,580), Miceli et al, for the reasons of record set forth in the previous office action mailed on 2/25/03.

Claims 27-33 are rejected under 35 U.S.C. 102(e) as being anticipated by Strulovici et al (US Patent 5,759,787), Miceli et al, for the reasons of record set forth in the previous office action mailed on 2/25/03.

***New Rejections necessitated by the Amendment***

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claim 39 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instant claim briefly recites a context-independent antibody that binds a single phospho-threonine residues and the antibody recognizes a plurality of peptides or proteins within a genome that contains the residue.

The specification in page 13 discloses that "motif-specific, context independent antibodies " means antibodies which are specific against one or more fixed amino acid residues in the context of variable surrounding peptide or protein sequences. The specification discloses antibodies which bind to specific motifs, ' RXS*XP; RSXS*XP; PXT*/S*PXR; acetylated lysine; RXRXXT*; RRXT*; and [F/Y][T*/S*] pr [S*/T*]F, which are not a representative of the claimed genus of context independent antibody that binds a singe phosphothreonine residue.

Further the specification discloses that the phosphothreonine antibodies bind all phosphothreonine containing sequences except those followed immediately in +1 position by proline. Thus the specification description clearly does not provide adequate representation regarding the open ended claim.

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that "written description of an invention involving a chemical genus, like a description a chemical species, 'requires precise definition, such as structure or formula or chemical name' of an the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1405 (1997), quoting Fiers v. Revel, 25 USPQ2d 1601, 1601 (Fed. Cir. 1993)* [ the claims at issue in University of California v. Eli Lilly defined the invention by function of the claimed DNA].

This holding is applicable to the present claimed product (antibodies) because the invention lacks showing of sufficient identifying characteristics or lacks examples of claimed product or, to demonstrate possession of claimed generic. The specification does not disclose the claimed genus antibodies. The pacification discloses antibodies which bind to specific motifs, not any antibody which bind to phosphothreonine. The specification does not have examples of all possible context independent antibodies that binds only a single phosphothreonine residue. Thus the specification lacks written description of the claimed invention.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 39 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 39 is vague and indefinite by reciting 'said antibody recognizing a plurality of peptides or proteins within a genome that contain said residue' it is not clear what does applicants mean by 'recognizing' does applicants mean the antibody binds several proteins with the residue. The term 'recognizing' does not mean binding. It is not clear what does applicants mean by recognizing, does it have a specific signal or react certain specific way (i.e., catalytic reaction). Applicants are requested to amend the claim.

Claim is vague indefinite by reciting 'antibody recognizing a plurality of peptides or proteins within a genome that contain said residue.' The recitation of 'protein or peptides within a genome' is vague since the genome does not have proteins or peptides. Does applicants mean all the proteins or peptide encoded by the genome. Applicants are requested to amend the claim. Further the genome does not contain the phosphothreonine residue as in the instant claims. If applicants mean peptides or proteins comprising 'phosphothreonine', applicants are requested to amend the claim.

Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term "proteins or peptides within a genome" in claim 39 is used by the claim to mean "multiple

peptides or proteins expressed from the genome of a given organism" (stated by applicants in the response filed on 8/8/03, page 15), while the accepted meaning is "proteins or peptides are not present within a genome" The term is indefinite because the specification does not clearly redefine the term.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claim 39 is rejected under 35 U.S.C. 102(e) as being anticipated by Tani et al (US patent 6,001,580).

The instant claim briefly recites a context-independent antibody that binds a single phosphothreonine residue and the antibody recognizes plurality of proteins or peptides that contain the residue.

The `580 patent discloses an anti-MAP kinase antibody capable of binding to amino cid sequence comprising phosphorylated threonine (SEQ ID NO: 1) (refers to the antibody that binds a single phosphothreonine residue of the instant claims). The reference discloses that the antibody binds to both ERK 1 and ERK2, which refers to context independent antibody of the instant claims. The reference antibody bind more than one protein which has phosphotreonine antibody, which would read on the instant claim limitation 'antibody binds to proteins or peptides containing the residue. Thus the reference clearly anticipates the claimed invention.

***Response to Arguments***

7. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

8. Applicant's arguments filed on 8/8/03, regarding the Written description rejection of claims, have been fully considered but they are not persuasive.

Applicants argue that "with respect to genus claim, no magic number of species need be described to satisfy the written description. Rather, the assessment of whether a "representative number" of species having the distinguishing characteristics and common elements of the claimed genus has been described in the specification remains in the eye of the – and from the standpoint of – the skilled artisan. What constitutes a "representative number" of species is an inverse function of the skill and knowledge in the art; the technique well developed in areas of technology (like antibody production) where the level of the skill is high, the technique well established and predictable, only a few exemplary species need be described to show possession of genus."

Applicants arguments have been considered and are not persuasive for the following reasons: a) the instant claims are not drawn to the methods of producing antibodies, which is well developed technology. The instant claims are drawn to genus of antibodies (products) which bind kinase consensus substrate or protein-protein binding motifs. The specification has not shown possession of the claimed genus of antibodies at the time of filing of the instant specification. b) The specification examples are drawn to antibodies which bind to specific motifs, 'phosphothreonine; RXS*XP; RSXS*XP; PXT*/S*PXR; acetylated lysine; RXRXXT*;

RRXT*; and [F/Y][T*/S*] pr [S*/T*]F. The disclosed antibodies which bind to the supra specific motifs do not represent the genus as claimed. c) applicants arguments regarding the "representative number of species" has been considered and are not persuasive because " when there is substantial variation within the genus, one must describe a sufficient variation within the genus to reflect the variation within the genus. For inventions in an unpredictable art, adequate written description of a genus embraces widely variant species can not be achieved by disclosing only one species within the genus. See e.g., Eli Lily (see MPEP 2163). In the instant application, the claims are drawn to antibodies. Even though the methods of antibody production is well established, the instant claims are drawn to antibodies which bind to specific motifs which is not a well established technology. The specification discloses how unpredictable the art is , i.e., the specification discloses that 'attempts to use the above mentioned techniques (methods for production of antibodies) to produce similar antibodies for phosphoserine or phosphothreonine havemet with limted success (see page 5). Thus raising or producing the claimed antibodies is not well known and is very unpredictable according to the back ground section of the specification. In the absence of sufficient teaching in the specification by structure or drawing showing the antibodies of the claimed invention a person skilled in the art would not be able to determine whether applicants are in possession of the claimed invention. The specification disclosure has not described or shown possession of the claimed antibodies.

An applicant may show possession of the invention by disclosure if drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention. See Vas Cath 935 F.2d at 1565, 19 USPQ2d at 1118.

Applicants argue that the presently claimed invention, in its broadest sense is a genus of antibodies having the following functional features: their binding affinity of "motif specific" but also "context independent," they bind either a "kinase consensus substrate motif" or " protein-protein binding motif", the bound motif comprises "at least one phosphorylated amino acid" and they bind a "plurality of peptides or proteins within a genome that contain the motif." For the inventions in emerging and unpredictable technologies, disclosure of only a method of making the invention and the function may not be sufficient to support a product claim. See e.g., Fiers v. Revel. 984 F.2d at 1169, 25 USPQ 2d at 1605. Thus, the rejections of record have been maintained for the reasons of record.

9. Applicant's arguments filed on 8/8/03, regarding the rejection of claim 28 as indefinite (B), have been fully considered but they are not persuasive. Applicants argue that 'Applicants have chosen to use the claim phrase " a plurality of peptides or proteins within a genome" to indicate a feature of the claimed class of antibody, namely the ability to bind multiple peptides or proteins expressed from the genome of a given organism." Applicant's response has been considered and is not persuasive, because if applicants mean 'the proteins or peptides expressed from a genome of a given organism', applicants should include in the claim. Further applicant's arguments regarding the 'genome' have been considered and are not persuasive since the arguments are not relevant to the rejection of record.

10. Applicant's arguments filed on 8/8/03, regarding the rejection of claims over Tani et al have been fully considered but they are not persuasive.

Applicants argue that the examiner has not properly construed the claimed subject matter

Based on the teachings of the specification. Applicants argue that the claimed invention in its broadest sense, is a genus of antibodies having the following features: their binding affinity of "motif specific" but also "context independent," they bind either a "kinase consensus substrate motif" or " protein-protein binding motif", the bound motif comprises "at least one phosphorylated amino acid" and they bind a "plurality of peptides or proteins within a genome that contain the motif." Applicants further argue according to applicants 'motif' is a short, modifiable amino acid motifs that are conserved among multiple different proteins in signal transduction cascades. The prior art (Tani et al) disclose antibodies which are specific to the MAP kinases. The reference disclose that the phosphorylation of two phosphorylation sites in MAP kinase ERK1 and ERK2. The reference MAP kinases would read on the motif of the instant claims. Further the meaning of 'motif' according to applicant's disclosure is a short, modifiable amino acid motifs that are conserved among multiple different proteins in signal transduction cascades, and the reference MAP kinases would read on the motifs of the instant claims. Further the reference specifically teaches amino acid sequence with phosphothreonine (SEQ ID NO: 1) to which the antibody binds (i.e., see column 4). Thus, the reference antibody clearly anticipates the claimed invention.

Applicants further argue that 'motif' of the instant invention mean 'short recurring motifs are distinct from the longer non-recurring typical unique modified epitopes bound by traditional site specific antibodies.' Applicant's arguments have been considered and however, the instant claims do not recite 'recurring short motif', and the instant claimed antibody binding to a motif comprising a phosphoryalted amino acid is open to antibodies which bind to specific epitopes. Thus the reference antibody which bind to the amino acid sequence comprising

phosphothreonine would read on the instant claims. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., recurring small signal transduction motifs) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant's arguments regarding the 'context independent' have been considered and are not persuasive. Applicants argue that the context independent antibodies specifically bind a recurring motifs conserved among multiple proteins. However, the reference discloses antibodies which bind amino acid sequence comprising phosphothreonine , and the antibody specifically binding to active form of human and rat MAP kinases (both ERK 1 and ERK2) (i.e., see column 4, lines 56-63) which refers to context independent antibodies of the instant claims. Thus the reference clearly anticipates the claimed invention. Applicants arguments regarding the 'reference does not teach the disclosed antibody is capable of binding to a plurality of different peptides or proteins within a genome that contains the motif' Is not persuasive because it is not clear what does applicants mean by proteins or peptides within a genome that contain a motif. The genome neither contain a peptide motif nor an amino acid motif. Thus the rejections of record have been maintained for the reasons of record.

11. Applicant's arguments filed on 8/8/03, regarding the rejection of claims over Strulovici et al have been fully considered but they are not persuasive.

Applicants argue that the examiner has misconstrued the meaning and scope of the

present claims, and mis read the teachings of the cited reference. Applicant's arguments have been fully considered and are not persuasive for the reasons discussed supra, regarding the interpretation and meaning of the instant claims. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the interpreted meaning of 'motif') are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The rejections of record have maintained for the reasons of record.

***Conclusion***

No claims are allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 703-305-3884. The examiner is on Flex Schedule and can normally reached from Monday through Friday between 7.30 AM and 4.00 PM..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 703-306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

Padmashri Ponnaluri
Primary Examiner
Art Unit 1639

Pp
11/11/03

PADMASHRI PONNALURI
PRIMARY EXAMINER